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p7.5tk

Not!

Apal

GGCCAAATTGAAAACTAGACTATTATTGACACGGGGCCGCATG GGC CCG GCC GCC AAC GGC GGC GGA
Met Gly Pro Ala Ala Asn Gly Gly

tk coding sequence

pE/Ltk

synthetic E/L promoter

Not!

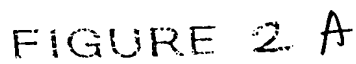
Apai

GGCCAAAATTGAAATTTTATTTTTTTTGGATATATAAAGCGGCCGCCATG GGC CCG GCC GCC AAC GGC GGA
Met Gly Pro Ala Asn Gly Gly

tk coding sequence

FIGURE 1

| Year | 1960 | 1961 | 1962 | 1963 | 1964 | 1965 | 1966 | 1967 | 1968 | 1969 | 1970 | 1971 | 1972 | 1973 | 1974 | 1975 | 1976 | 1977 | 1978 | 1979 | 1980 | 1981 | 1982 | 1983 | 1984 | 1985 | 1986 | 1987 | 1988 | 1989 | 1990 | 1991 | 1992 | 1993 | 1994 | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 | 2026 | 2027 | 2028 | 2029 | 2030 | 2031 | 2032 | 2033 | 2034 | 2035 | 2036 | 2037 | 2038 | 2039 | 2040 | 2041 | 2042 | 2043 | 2044 | 2045 | 2046 | 2047 | 2048 | 2049 | 2050 | 2051 | 2052 | 2053 | 2054 | 2055 | 2056 | 2057 | 2058 | 2059 | 2060 | 2061 | 2062 | 2063 | 2064 | 2065 | 2066 | 2067 | 2068 | 2069 | 2070 | 2071 | 2072 | 2073 | 2074 | 2075 | 2076 | 2077 | 2078 | 2079 | 2080 | 2081 | 2082 | 2083 | 2084 | 2085 | 2086 | 2087 | 2088 | 2089 | 2090 | 2091 | 2092 | 2093 | 2094 | 2095 | 2096 | 2097 | 2098 | 2099 | 2100 |
|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| 1960 | 1961 | 1962 | 1963 | 1964 | 1965 | 1966 | 1967 | 1968 | 1969 | 1970 | 1971 | 1972 | 1973 | 1974 | 1975 | 1976 | 1977 | 1978 | 1979 | 1980 | 1981 | 1982 | 1983 | 1984 | 1985 | 1986 | 1987 | 1988 | 1989 | 1990 | 1991 | 1992 | 1993 | 1994 | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 | 2026 | 2027 | 2028 | 2029 | 2030 | 2031 | 2032 | 2033 | 2034 | 2035 | 2036 | 2037 | 2038 | 2039 | 2040 | 2041 | 2042 | 2043 | 2044 | 2045 | 2046 | 2047 | 2048 | 2049 | 2050 | 2051 | 2052 | 2053 | 2054 | 2055 | 2056 | 2057 | 2058 | 2059 | 2060 | 2061 | 2062 | 2063 | 2064 | 2065 | 2066 | 2067 | 2068 | 2069 | 2070 | 2071 | 2072 | 2073 | 2074 | 2075 | 2076 | 2077 | 2078 | 2079 | 2080 | 2081 | 2082 | 2083 | 2084 | 2085 | 2086 | 2087 | 2088 | 2089 | 2090 | 2091 | 2092 | 2093 | 2094 | 2095 | 2096 | 2097 | 2098 | 2099 | 2100 | |



B

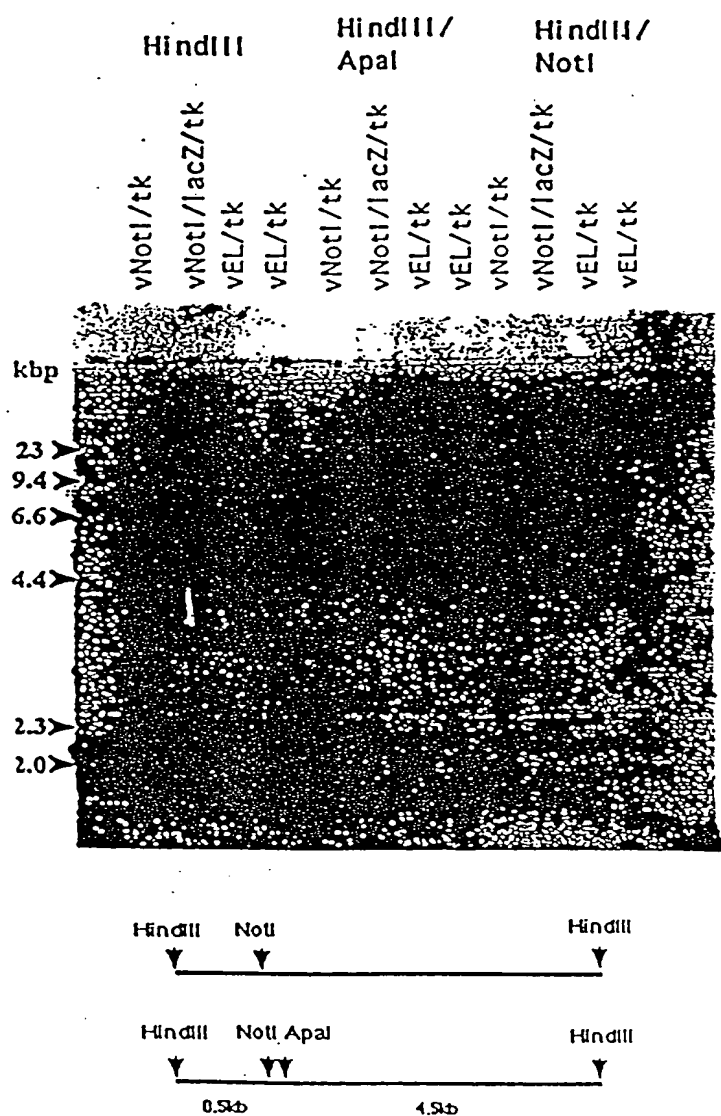


FIGURE 2B

Apal NotI

λ WR WR vEL v7.5 vNotI/k
 WR vEL v7.5 vNotI/k



WR

NotI

vNotI/k

NotI

vEL/k

v7.5/k

NotI Apal

FIGURE 3

Phi X
WR
pJNot
vNotI/tk
vpNotI
p7.5/tk
v7.5/tk
vNotI/lacZ/tk
pEL/tk
vEL/tk

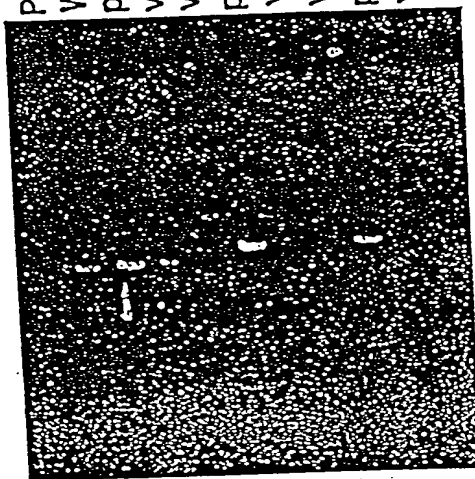


FIGURE 4

B-Glucoronidase Analysis of Recombinant Viruses

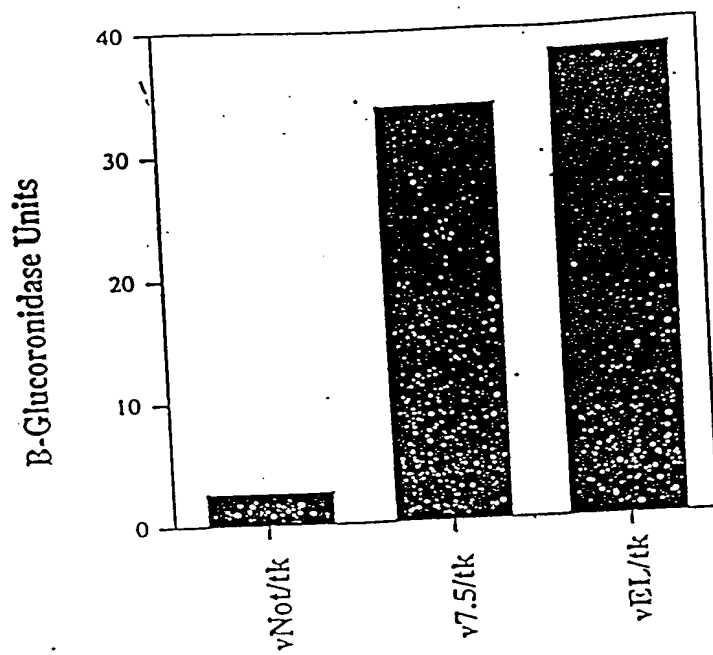


FIGURE 5

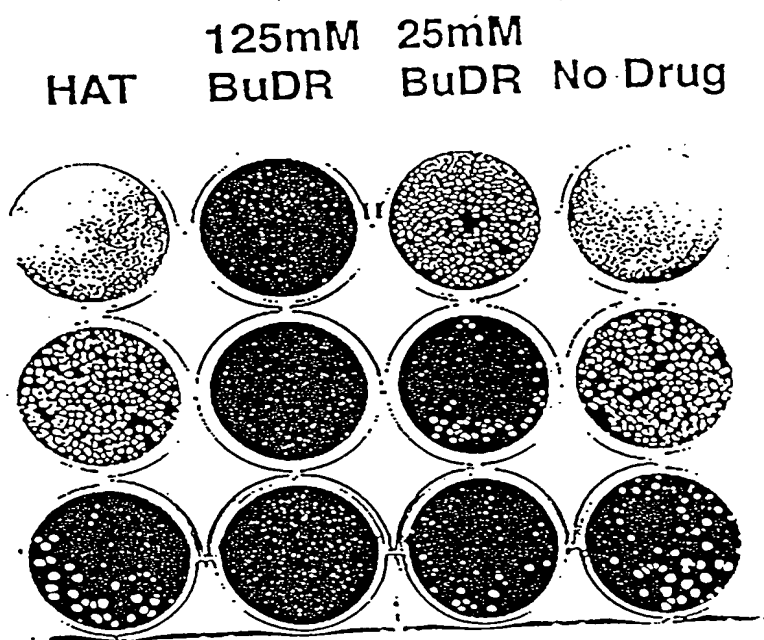


FIGURE 6

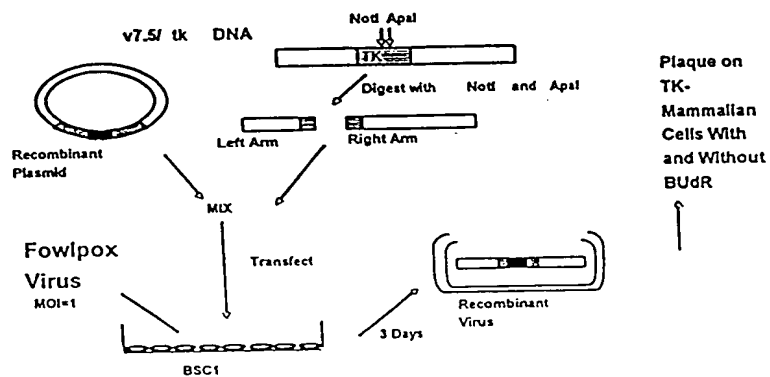


FIGURE 7

1. p7.5tk

5'-GGCCAAAATTGAAAACTAGATCTATTATTGCACGCGCGCCATGGCCCGGCC-3'

2. p7.5/ATG0/tk

5'-GGCCAAAAATTGAAAAAAGTCTATTATTGCACGGCGCGCGCGTGGATCCCCGGGGCTGCAGGAA

| | TRANSCRIPTION | STOP SIGNAL |
|------|---------------|-------------|
| | TRANSLATION | STOP CODONS |
| SALI | | |

TTTGATATCAAGCTTATCGATACCGTCGACCTCGAGGGGGCCCTAACTAACTAATTTGTTTTTGT

APAI

GGGCCCGGC-3'

3. p7.5/ATG1/hk

| 7.5K PROMOTER | NOTI | START | CODON BAMHI | SMAI | PSTI |
|---------------------|-----------|-------------|-------------|---------|------------|
| 5'-GGCCAAAATTGAAAAC | TATTTATTG | CACGCGGCCCA | TGGTGGAT | CCCCCGG | GCTGCAGGAA |

| TRANSLATION | TRANSCRIPTION |
|-------------|---------------|
|-------------|---------------|

| SALI | STOP CODONS | STOP SIGNAL |
|------|-------------|-------------|
|------|-------------|-------------|

TTCGATATCAAGCTTATCGATACCGTCGACCTCGAGGGGGGCCCTAACTAATTTGTTTTGT

APAI

GGGCCCGGCC-3'

4. p7.5/ATG2/tk

5'- GGCCAAAAATTGAAAACTAGATCTATTATTGCACGGCGCGGCCCA TGAGTGGATCCCCCGGCTGCAGGA

| TRANSCRIPTION | TRANSLATION |
|----------------|-------------|
| STOP SIGNAL | STOP CODONS |
| 3'-ACTAATTTTGT | |

SALI

SALI
TTGGATATCAAGCTTATCGATACCGTCGACCTCGAGGGGGCCTAACATAATTGTTTGT

APAI

GGGCCGCC-3'

[illegible]

| | | | | |
|---|-------|-------------|---------------|------|
| | START | CODON | BAMHI SMAI | PSTI |
| 5. p7.5/ATG3/tk | | | | |
| | NOTI | | | |
| 7.5K PROMOTER | | | | |
| 5'- GGCCAAAATTGAAAAACTAGATCTATTTATTGCACGGCGGCCGcA TGACGTGGATCCCCCGGCTGCAGGA | | | | |
| | | TRANSLATION | TRANSCRIPTION | |
| | | STOP CODONS | STOP SIGNAL | |
| SALI | | | | |
| TTCGATATCAAGCTTATCGATAccGTcGAcCtCGAGGGGGGcCTAAcTAActTTGTTTTGT | | | | |

APAI

GGGCCGCC-3'

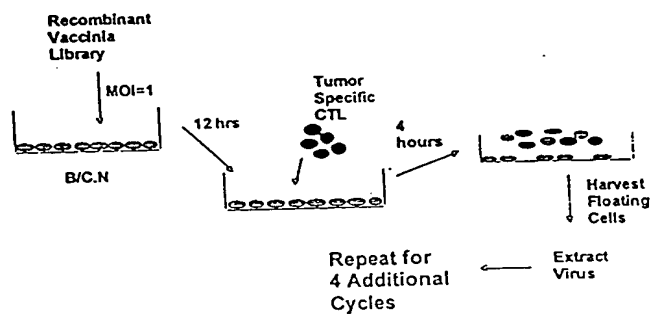


FIGURE 9

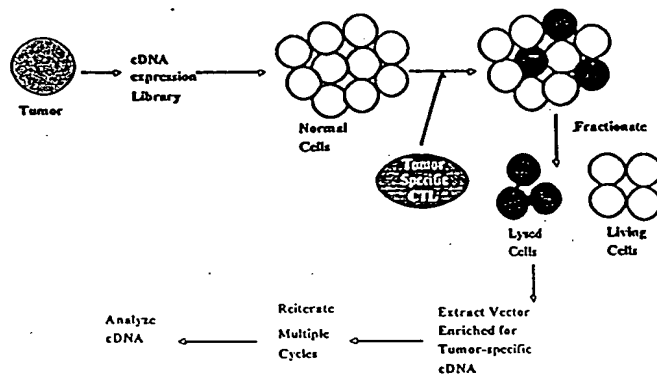


FIGURE 10

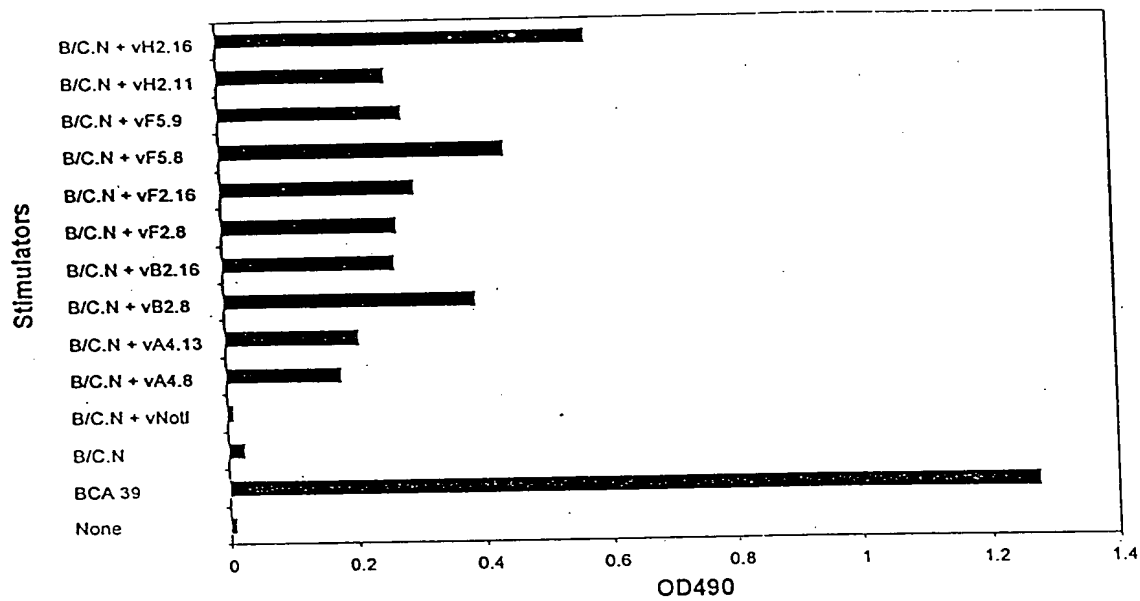


FIGURE IIA

| <u>Target</u> | Percent Specific Lysis | |
|-------------------------|------------------------|------------|
| | Effector : Target | |
| | <u>10:1</u> | <u>2:1</u> |
| BCA 34 | 68.4 | 54.8 |
| BCA 39 | 36.6 | 23.4 |
| B/C.N | 0.2 | 0.3 |
| B/C.N + vF5.8 | 47.5 | 34.6 |
| B/C.N + vH2.16 | 67.8 | 56.2 |
| B/C.N + vaccinia vector | 0 | 0.2 |

FIGURE 11B

A. L3

| | | | | | | | | | | | | | | | |
|------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|--|
| Amino Acid | | | | | | | | | | | | | | | |
| Position | 45 | 46 | 47 | 48 | 49 | 50 | 51 | 52 | 53 | 54 | 55 | 56 | | | |
| Sequence | A | F | L | G | Y | K | A | G | M | T | H | I | | | |
| Nucleotide | GCC | TTT | CTG | GGT | TAC | AAG | GCT | GGC | ATG | ACC | CAC | ATC | | | |

B. H2.16

| | | | | | | | | | | | | | | | |
|------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|--|
| Amino Acid | | | | | | | | | | | | | | | |
| Position | 45 | 46 | 47 | 48 | 49 | 50 | 51 | 52 | 53 | 54 | 55 | 56 | | | |
| Sequence | A | F | L | G | Y | K | A | G | M | I | H | I | | | |
| Nucleotide | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | -T- | --- | | | |

FIGURE 12

Percent Specific Lysis

Effector: Target

| <u>Target</u> | <u>10:1</u> | <u>2:1</u> |
|-------------------------------|-------------|------------|
| BCA 34 | 62.4 | 32.1 |
| BCA 39 | 49.7 | 23.6 |
| B/C.N | 3.3 | 0.2 |
| B/C.N + L3 peptide 48-56(I54) | 46.0 | 16.1 |
| B/C.N + L3 peptide 48-56(T54) | 2.0 | 0 |
| B/C.N + L3 peptide 45-54(I54) | 0 | 0 |

FIGURE 13A

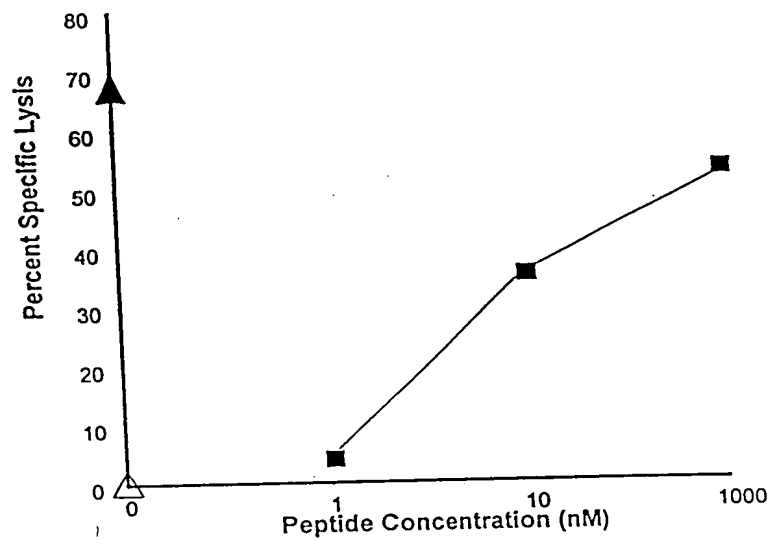
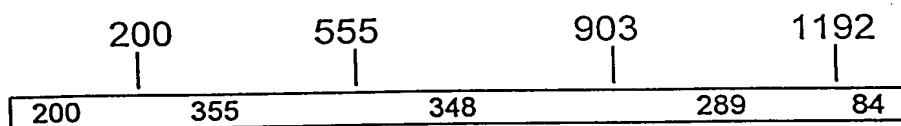


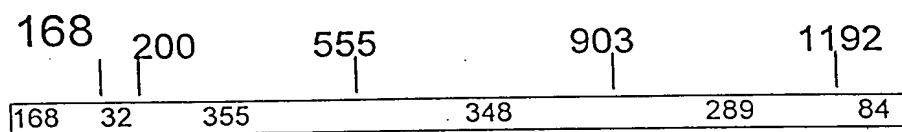
FIGURE 13B

Published L3 (1276 bp)



168-171 = GACC

H2.16 (1276 bp)



168-171 = GATC

FIGURE 14A

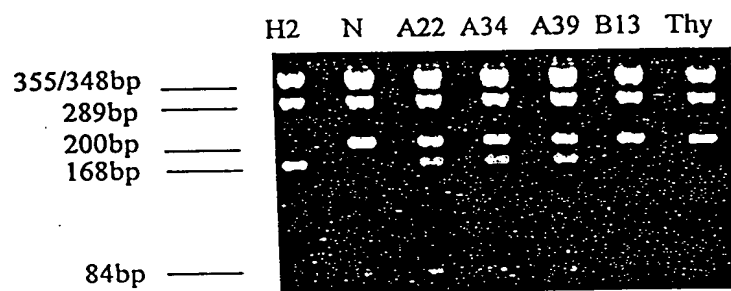


FIGURE 14B

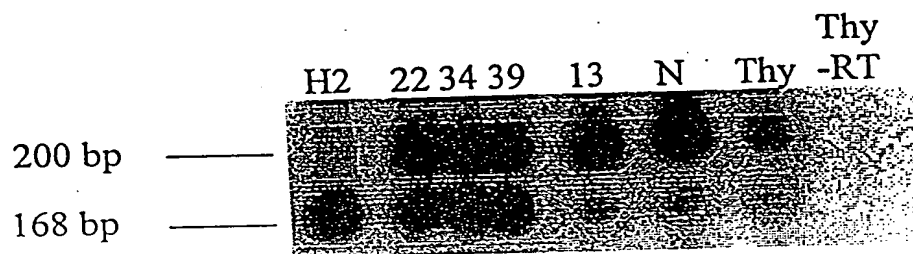


FIGURE 14C

| <u>Target</u> | Percent Specific Lysis Immunogen | | | |
|------------------------|-------------------------------------|-------------|-------------|-------------|
| | vH2.16 | | v7.5/tk | |
| | <u>40:1</u> | <u>10:1</u> | <u>40:1</u> | <u>10:1</u> |
| BCA 34 | 33.6 | 12.9 | 5.7 | 4.0 |
| BCA 39 | 22.1 | 9.0 | 5.3 | 3.1 |
| B/C.N + L3 48-56 (I54) | 48.2 | 20.2 | 3.9 | 1.5 |
| B/C.N + L3 48-56 (T54) | 6.4 | 1.4 | 1.8 | 2.9 |
| B/C.N | 7.1 | 5.7 | 6.1 | 2.8 |
| YAC | 1.2 | 2.5 | 0 | 1.8 |

FIGURE 15 A

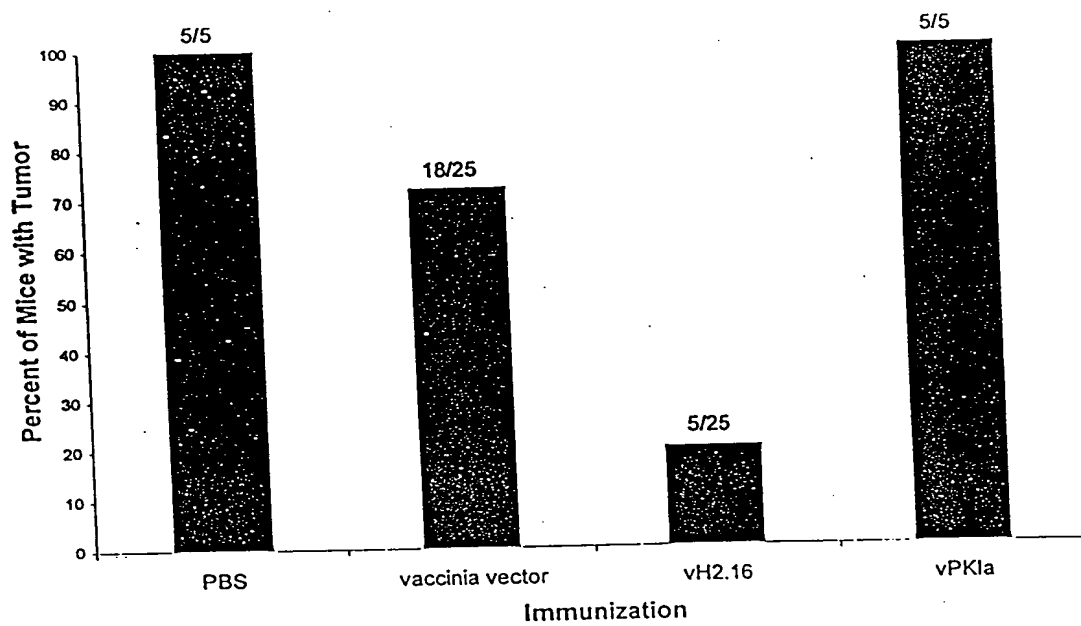


FIGURE 15B

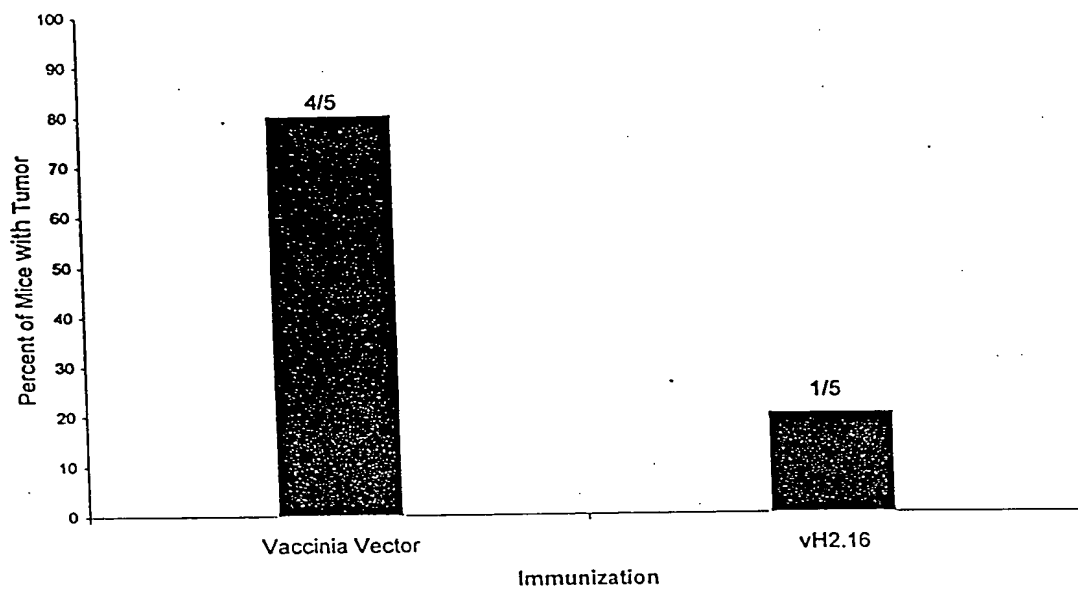


FIGURE 15C

A. Influenza Specific Cytolytic Activity of CD4+
CD45RA+ Human T Cells Stimulated in the Presence
of IL-12 and IL-18.

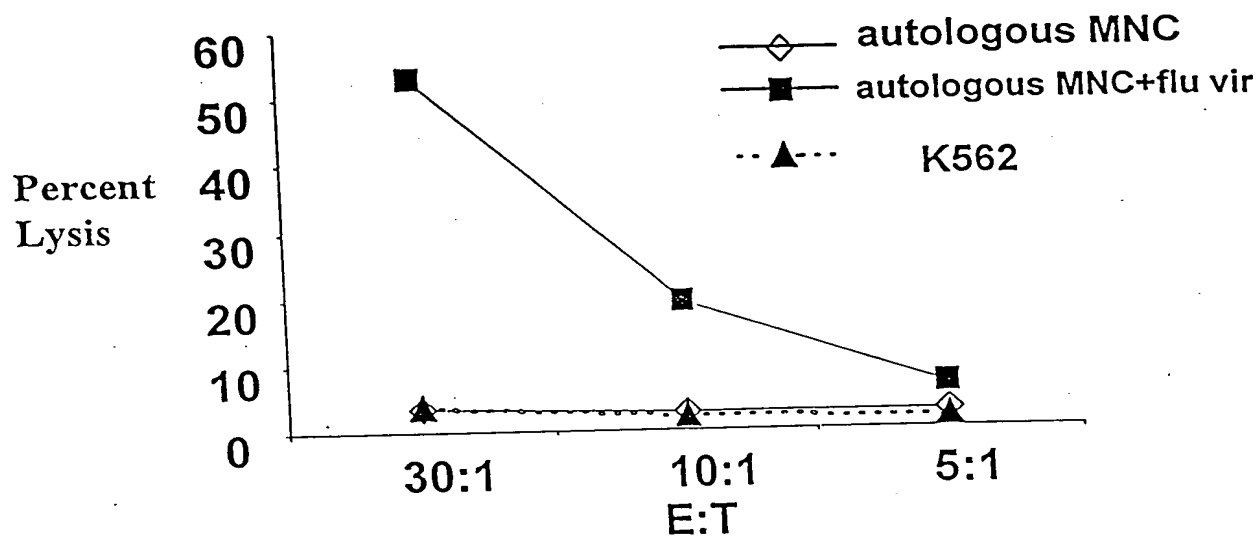
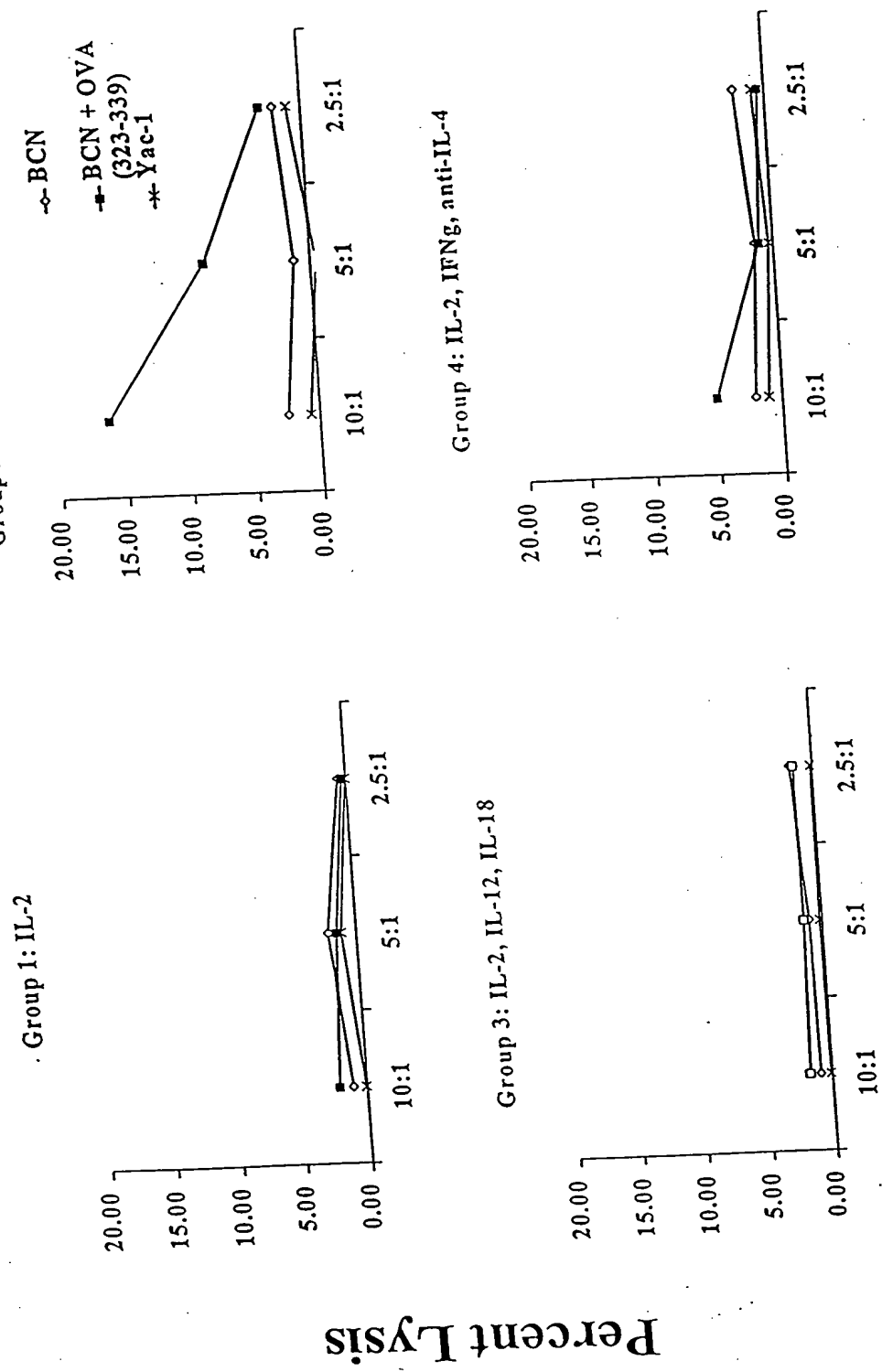


FIGURE 16

CD4+ Primary Cytotoxic T Cell response



E:T

FIGURE 17

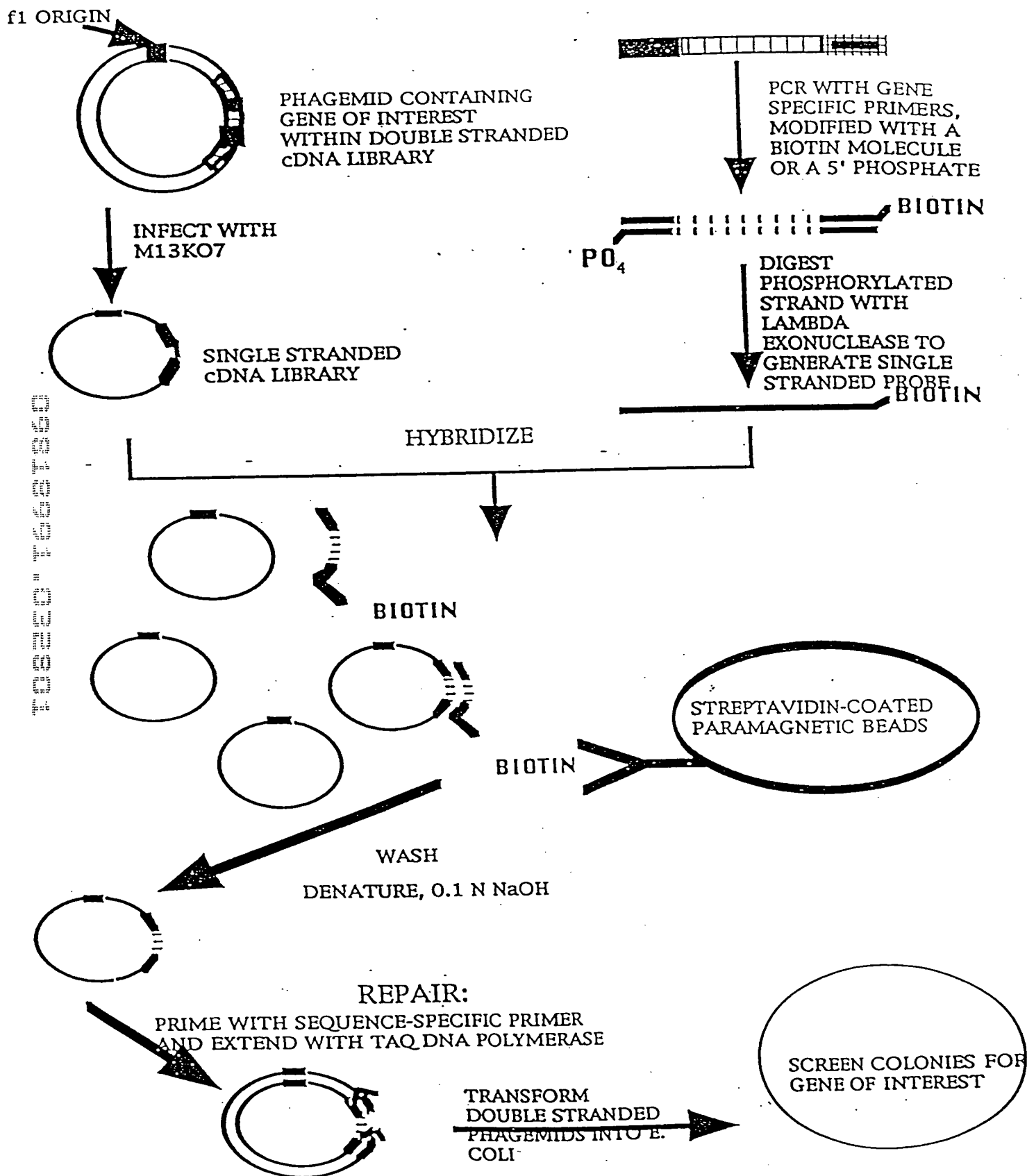


FIGURE 18

Herceptin (anti-Her2/neu) antibody sensitizes SK-BR-3 cells to antibody-dependent cellular cytotoxicity (ADCC)

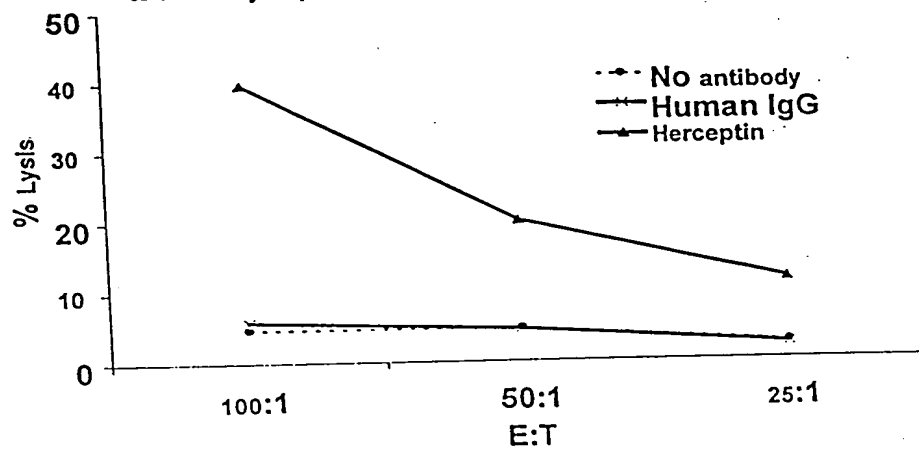


FIGURE 19

Tolerance to Alloantigens Induced in presence of Antigens and Anti-CD40 Ligand Antibody

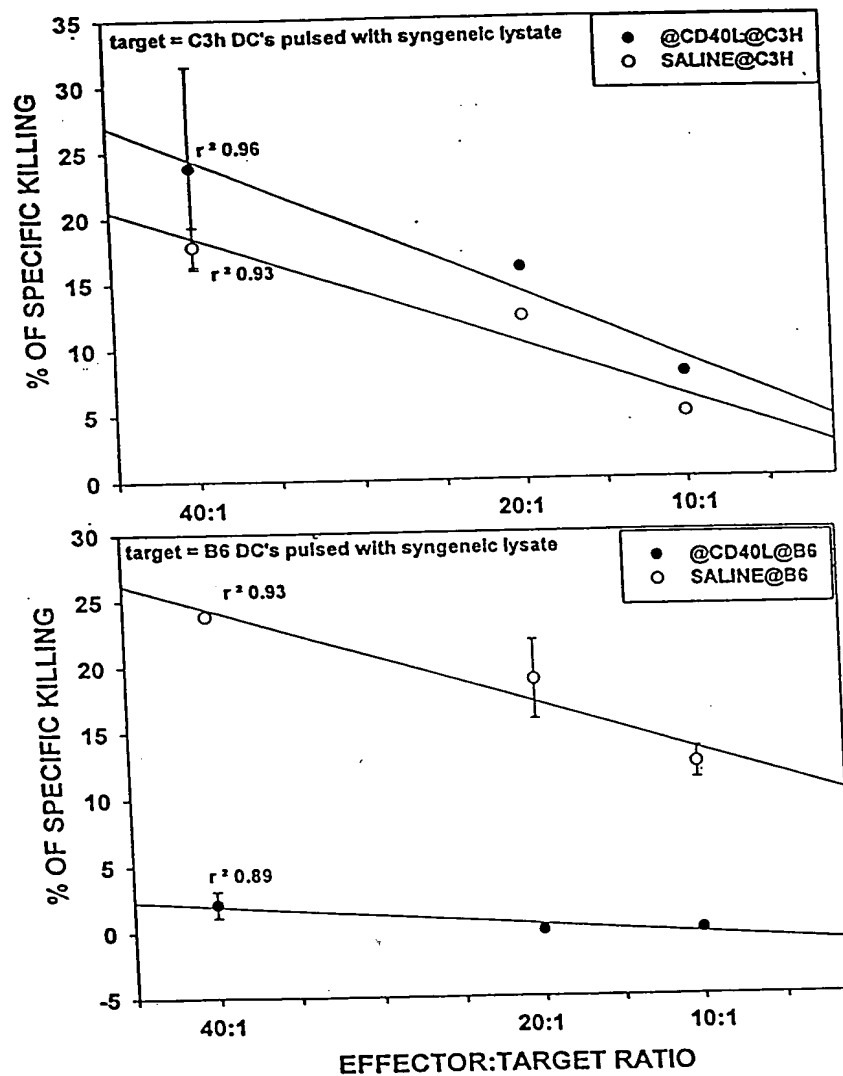


FIGURE 20

Figure 21

| | | | | |
|-------------|------------|---|---|---|
| Hydroxyurea | — | — | — | + |
| BMP-2 | — | + | + | + |
| | Col Type X | | | |
| | GAPDH | | | |